

(FILE 'CAPLUS' ENTERED AT 12:26:39 ON 30 DEC 2003)

L3 24 S (PARAMYXOVIRUS (W) (HEMAGGLUTININNEURAMINIDASE OR HEMAGGLUTI

FILE 'CAPLUS, MEDLINE' ENTERED AT 12:32:55 ON 30 DEC 2003

L4 24 FILE CAPLUS

L5 20 FILE MEDLINE

TOTAL FOR ALL FILES

L6 44 S L3

L7 25 DUPLICATE REMOVE L6 (19 DUPLICATES REMOVED)

=> d bib,abs 7-11,16,21

L7 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1999:64941 CAPLUS

DN 130:122133

TI Epitopes and active sites of paramyxoviridae proteins and uses thereof

IN Langedijk, Johannes Petrus Maria; Van Oirschot, Johannes Theodorus

PA Stichting Instituut voor Dierhouderij en Diergezondheid, Neth.

SO PCT Int. Appl., 63 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9902695	A2	19990121	WO 1998-NL390	19980708
	WO 9902695	A3	19990408		
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	AU 9882462	A1	19990208	AU 1998-82462	19980708
PRAI	EP 1997-202100	A	19970708		
	WO 1998-NL390	W	19980708		

AB The invention relates to the field of paramyxoviridae, vaccines against infections by such viruses, diagnostics for detecting such viruses and targets for therapeutics against such viruses. In particular, the invention relates to 3-D models identifying a proteinaceous substance comprising at least one virus epitope derived from the attachment protein of a virus from the family of paramyxoviridae, said epitope corresponding to an antigenic site present on the HN protein of paramyxovirus, which site is identified as one of loop .beta.1L01, .beta.1L23, .beta.2L01, .beta.2L23, .beta.3L01, .beta.3L23, .beta.4L01, .beta.4L23, .beta.5L01, .beta.5L23, .beta.6L01 and .beta.6L23, or a functional equiv. thereof. Also, the invention relates to a substance blocking the enzymic activity of the morbillivirus H protein. As an example, sialic acid was used to block the activity of the H protein.

L7 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN

AN 1999:188573 CAPLUS

DN 130:335232

TI Amino acid substitutions in a conserved region in the stalk of the Newcastle disease virus HN glycoprotein spike impair its neuraminidase activity in the globular domain

AU Wang, Zhiyu; Iorio, Ronald M.

CS Department of Molecular Genetics and Microbiology, University of Massachusetts Medical School, Worcester, MA, 01655-0122, USA

SO Journal of General Virology (1999), 80(3), 749-753

CODEN: JGVIAIY; ISSN: 0022-1317

PB Society for General Microbiology  
DT Journal  
LA English

AB The ectodomain of the **paramyxovirus hemagglutinin-neuraminidase** (HN) glycoprotein spike can be divided into two regions: a membrane-proximal, stalk-like structure and a terminal globular domain. The latter contains all the antibody recognition sites of the protein, as well as its receptor recognition and neuraminidase (NA) active sites. These two activities of the protein can be sep'd. by monoclonal antibody functional inhibition studies and mutations in the globular domain. Herein, we show that mutation of several conserved residues in the stalk of the Newcastle disease virus HN protein markedly decrease its NA activity without a significant effect on receptor recognition. Thus, mutations in the stalk, distant from the NA active site in the globular domain, can also sep. attachment and NA. These results add to an increasing body of evidence that the NA activity of this protein is dependent on an intact stalk structure.

RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 5

AN 1999:538410 CAPLUS

DN 131:348236

TI Anomeric Specificity and Protein-Substrate Interactions Support the 3D Model for the Hemagglutinin-Neuraminidase from Sendai Virus

AU Bellini, Tiziana; Pasti, Claudia; Manfrinato, Maria Cristina; Tomasi, Maurizio; Dallochio, Franco

CS Dipartimento di Biochimica e Biologia Molecolare, Universita di Ferrara, Ferrara, 44100, Italy

SO Biochemical and Biophysical Research Communications (1999), 262(2), 401-405

CODEN: BBRCA9; ISSN: 0006-291X

PB Academic Press

DT Journal

LA English

AB The 3D structure of **paramyxovirus hemagglutinin-neuraminidase** has not yet been resolved; however, a theor. model has been built by using influenza virus and bacterial neuraminidases as template. Two common features of the catalytic mechanism of the neuraminidases of known 3D structure are the anomeric specificity and the involvement of a tyrosine residue in the stabilization of the transition state. These key features have been investigated on the water-sol. ectodomain of the hemagglutinin-neuraminidase from Sendai virus (cHN). The anomeric specificity of the hydrolysis of the substrate by cHN has been investigated by NMR spectroscopy. The immediate product of the reaction was the .alpha.-anomer, meaning that cHN belongs to glycohydrolases retaining anomeric configuration like influenza virus neuraminidase. Measurements of the UV difference spectrum upon binding of the substrate analog 2,3-dehydro 2-deoxy N-acetyl neuraminic acid indicate the ionization of a tyrosine residue and decreased polarity in the environment of a tryptophan residue. Functional significance of the spectral data was derived from the known structure of influenza neuraminidase, where a tyrosinate ion is involved in the stabilization of the transition-state carbonium ion, and a tryptophan residue is involved in the binding of the acetyl moiety of the substrate. The data give exptl. support to the 3D model of paramyxovirus neuraminidase. (c) 1999 Academic Press.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 6

AN 1997:465434 CAPLUS

DN 127:187297

TI Sequence and structure alignment of Paramyxoviridae attachment proteins

and discovery of enzymic activity for a morbillivirus hemagglutinin  
 AU Langedijk, Johannes P. M.; Daus, Franz J.; van Oirschot, Jan T.  
 CS Dep. of Mammalian Virology, Institute for Animal Science and Health,  
 Lelystad, Neth.  
 SO Journal of Virology (1997), 71(8), 6155-6167  
 CODEN: JOVIAM; ISSN: 0022-538X  
 PB American Society for Microbiology  
 DT Journal  
 LA English  
 AB On the basis of the conservation of neuraminidase (N) active-site residues  
 in influenza virus N and **paramyxovirus hemagglutinin-  
 neuraminidase** (HN), it has been suggested that the  
 three-dimensional (3D) structures of the globular heads of the two  
 proteins are broadly similar. In this study, details of this structural  
 similarity are worked out. Detailed multiple sequence alignment of  
 paramyxovirus HN proteins and influenza virus N proteins was based on the  
 schematic representation of the previously proposed structural similarity.  
 This multiple sequence alignment of paramyxovirus HN proteins was used as  
 an intermediate to align the morbillivirus hemagglutinin (H) proteins with  
 neuraminidase. Hypothetical 3D structures were built for paramyxovirus HN  
 and morbillivirus H, based on homol. modeling. The locations of  
 insertions and deletions, glycosylation sites, active-site residues, and  
 disulfide bridges agree with the proposed 3D structure of HN and H of the  
 Paramyxoviridae. Moreover, details of the modeled H protein predict  
 previously undescribed enzymic activity. This prediction was confirmed  
 for rinderpest virus and peste des petits ruminants virus. The enzymic  
 activity was highly substrate specific, because sialic acid was released  
 only from crude mucins isolated from bovine submaxillary glands. The  
 enzymic activity may indicate a general infection mechanism for  
 respiratory viruses, and the active site may prove to be a new target for  
 antiviral compds.

L7 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 7  
 AN 1997:729261 CAPLUS  
 DN 128:58937

TI Modeling the **paramyxovirus hemagglutinin-  
 neuraminidase** protein

AU Epa, V. Chandana  
 CS Biomolecular Research Institute, Parkville, 3052, Australia  
 SO Proteins: Structure, Function, and Genetics (1997), 29(3), 264-281  
 CODEN: PSFGY; ISSN: 0887-3585  
 PB Wiley-Liss  
 DT Journal  
 LA English

AB The **paramyxovirus hemagglutinin-neuraminidase**  
 (HN) protein exhibits neuraminidase activity and has an active site  
 functionally similar to that in influenza neuraminidases. Earlier work  
 identified conserved amino acids among HN sequences and proposed  
 similarity between HN and influenza neuraminidase sequences. In this work  
 we identify the three-dimensional fold and develop a more detailed model  
 for the HN protein, in the process we examine a variety of protein  
 structure prediction methods. We use the known structures of viral and  
 bacterial neuraminidases as controls in testing the success of protein  
 structure prediction and modeling methods, including knowledge-based  
 threading, discrete three-dimensional environmental profiles, hidden  
 Markov models, neural network secondary structure prediction, pattern  
 matching, and hydropathy plots. The results from threading show that the  
 HN protein sequence has a 6 .beta.-sheet propeller fold and enable us to  
 assign the locations of the individual .beta.-strands. The  
 three-dimensional environmental profile and hidden Markov model methods  
 were not successful in this work. The model developed in this work helps  
 to understand better the biol. function of the HN protein and design  
 inhibitors of the enzyme and serves as an assessment of some protein  
 structure prediction methods, esp. after the x-ray crystallog. soln. of

its structure.

RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD  
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 16 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 11

AN 1994:506183 CAPLUS

DN 121:106183

TI Site-directed mutagenesis of a conserved hexapeptide in the

**paramyxovirus hemagglutinin-neuraminidase**

glycoprotein: effects on antigenic structure and function

AU Mirza, Anne M.; Deng, Ruitang; Iorio, Ronald M.

CS Medical School, University of Massachusetts, Worcester, MA, 01655, USA

SO Journal of Virology (1994), 68(8), 5093-9

CODEN: JOVIAM; ISSN: 0022-538X

DT Journal

LA English

AB The sequence NRKSCS constitutes the longest linear stretch in the amino acid sequence of the hemagglutinin-neuraminidase (HN) glycoprotein of the paramyxoviruses that is completely conserved among all viruses in the group. The authors have used site-directed mutagenesis and expression of the mutated HN protein of one member of the group, Newcastle disease virus, to explore the role of this highly conserved sequence in the structure and function of the protein. Any substitution introduced for each of 4 residues in the sequence, N-234, R-235, K-236, or S-237, results in a drastic decrease in neuraminidase activity relative to that of the wild-type protein. Only substitutions for the terminal serine residue in the sequence had comparatively little effect on this activity. These findings are consistent with prior computer-based predictions of protein secondary structure which had suggested that this domain corresponds to one in the .beta.-sheet propeller structure of the neuraminidase protein of influenza virus closest to the center of the sialic acid binding site and forms part of the enzyme active site. Four of the substitutions, N-234.fwdarw.Y and K-236.fwdarw.E, .fwdarw.Q, and .fwdarw.S, apparently cause a local alteration in the antigenic structure of the protein. This is evidenced by (i) the diminished recognition of the protein only by monoclonal antibodies thought to bind at the neuraminidase active site, among an extensive panel of conformation-specific antibodies, and (ii) the slower rate of migration in SDS-PAGE for all except the K-236.fwdarw.Q mutation. One of the mutations, K-236.fwdarw.S, completely abolishes the ability of the protein to promote cellular fusion when coexpressed with the fusion protein. The latter cannot be explained by a decrease in the relative hemadsorption activity of the protein and suggests that the globular head of the protein may contribute to this process beyond providing receptor recognition.

L7 ANSWER 21 OF 25 CAPLUS COPYRIGHT 2003 ACS on STN DUPLICATE 16

AN 1991:39783 CAPLUS

DN 114:39783

TI Folding and oligomerization properties of a soluble and secreted form of the **paramyxovirus hemagglutinin-neuraminidase** glycoprotein

AU Parks, Griffith D.; Lamb, Robert A.

CS Dep. Biochem., Mol. Biol. Cell Biol., Northwestern Univ., Evanston, IL, 60208-3500, USA

SO Virology (1990), 178(2), 498-508

CODEN: VIRLAX; ISSN: 0042-6822

DT Journal

LA English

AB The paramyxovirus SV5 hemagglutinin-neuraminidase (HN) glycoprotein (a type II integral membrane protein) was converted into a sol. and secreted form (HN-F) by replacing the HN signal/anchor domain with a hydrophobic domain that can act as a cleavable signal sequence. Approx. 40% of the HN-F synthesized was secreted from cells (t1/2 .apprx. 2.5-3 h). The extracellular HN-F mols. were identified as disulfide-linked dimers and

the majority of the population of mols. were resistant to endoglycosidase H digestion. Examn. of the oligomeric form of the secreted HN-F, by sucrose d. gradient sedimentation, indicated that under conditions where HN was a tetramer, HN-F was found to be a dimer, and no extracellular HN-F monomeric species could be detected. Secreted HN-F was fully reactive with conformation-specific monoclonal antibodies and was enzymically active as shown by HN-F having neuraminidase activity. Examn. of the intracellular HN-F species indicated that HN-F monomers were slowly converted to the disulfide-linked form and that under the sucrose d. gradient sedimentation conditions used the HN-F monomers aggregated. Some of the HN-F monomers were degraded intracellularly. These data are discussed in relationship to the seemingly different folding and oligomerization requirements for the intracellular transport of sol. and membrane-bound forms of a glycoprotein. The sol. and biol. active form of HN may be suitable for further structural and enzymic studies